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Attorney's Docket No.: 07039-129001

#16/B
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Jens Ponikau
Serial No. : 09/177,273
Filed : October 22, 1998
Title : METHODS AND MATERIALS FOR TREATING AND PREVENTING INFLAMMATION OF MUCOSAL TISSUE

Art Unit : 1614
Examiner : Kevin Weddington

Commissioner for Patents
Washington, D.C. 20231

AMENDMENT

In response to the action mailed April 11, 2000, please amend the application as follows:

In the Claims

Please cancel claims 8, 14, and 15 without prejudice.

Please amend claims 1 and 7 as follows:

1. (Once Amended) A method for treating a mammal having non-invasive fungus-induced intestinal mucositis, comprising mucoadministering to the digestive tract of said mammal a formulation in an amount, at a frequency, and for a duration effective to reduce or eliminate said non-invasive fungus-induced intestinal mucositis, said formulation comprising an antifungal agent, wherein said mucoadministration comprises orally applying said formulation to said digestive tract, and wherein said duration is greater than about 30 days.

7. (Once Amended) The method of claim 1, wherein said formulation is in a solid[, liquid, or aerosol] form.

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I hereby certify under 37 CFR §1 8(a) that this correspondence is being deposited with the United States Postal Service as first class mail with sufficient postage on the date indicated below and is addressed to the Commissioner for Patents, Washington, D C. 20231.

September 11, 2000
Date of Deposit

Jill Huso
Signature

Jill Huso
Typed or Printed Name of Person Signing Certificate

77

Please add claims 51-104 as follows:

18
51. The method of claim 1, wherein said antifungal agent comprises an antifungal agent selected from the group consisting of ketoconazole, itraconazole, saperconazole, and voriconazole.

19
52. The method of claim 1, wherein said antifungal agent comprises amphotericin B.

20
53. The method of claim 1, wherein said antifungal agent comprises itraconazole.

21
54. The method of claim 1, wherein said formulation comprises about 0.01 ng to about 1000 mg of said antifungal agent.

22
55. The method of claim 1, wherein said formulation comprises about 1 ng to about 500 mg of said antifungal agent.

23
56. The method of claim 1, wherein said formulation comprises about 100 mg of said antifungal agent.

24
57. The method of claim 1, wherein said formulation comprises a plurality of antifungal agents.

25
58. The method of claim 1, wherein said effective amount of said formulation comprises about 0.01 ng to about 1000 mg of said antifungal agent per kg of body weight of said mammal.

26
59. The method of claim 1, wherein said effective amount of said formulation comprises about 1 ng to about 500 mg of said antifungal agent per kg of body weight of said mammal.

27
60. The method of claim 1, wherein said effective amount of said formulation remains constant during said effective duration.

28
61. The method of claim 1, wherein said effective frequency of said mucoadministration is from about four times a day to about once every other week.

29
62. The method of claim 1, wherein said effective frequency of said mucoadministration is from about twice a day to about once a week.

30
63. The method of claim 1, wherein said effective frequency of said mucoadministration is more frequent than once a day.

31
64. The method of claim 1, wherein said effective frequency of said mucoadministration is more frequent than once a week.

32
65. The method of claim 1, wherein said effective duration is greater than about 60 days.

33
66. The method of claim 1, wherein said effective duration is greater than about 90 days.

34
67. The method of claim 1, wherein said formulation comprises a compound selected from the group consisting of pharmaceutically acceptable aqueous vehicles, pharmaceutically acceptable solid vehicles, mucolytic agents, antibacterial agents, anti-inflammatory agents, immunosuppressants, dilators, vaso-constrictors, steroids, and therapeutic compounds.

35
68. The method of claim 1, wherein said method comprises administering to said mammal a second formulation.

36
69. The method of claim 35, wherein said second formulation comprises a compound selected from the group consisting of antifungal agents, pharmaceutically acceptable aqueous vehicles, pharmaceutically acceptable solid vehicles, mucolytic agents, antibacterial agents, anti-inflammatory agents, immunosuppressants, dilators, vaso-constrictors, steroids, and therapeutic compounds.

37 ~~70.~~ The method of claim 1, said method comprising, after said mucoadministration, prophylactically mucoadministering to said mammal a prophylactic formulation in an amount, at a frequency, and for a duration effective to prevent said non-invasive fungus-induced intestinal mucositis, said prophylactic formulation comprising an antifungal agent.

38 ~~71.~~ The method of claim 37 ~~70~~, wherein said prophylactic mucoadministration comprises direct mucoadministration.

39 ~~72.~~ A method for prophylactically treating a mammal at risk for developing non-invasive fungus-induced intestinal mucositis, comprising mucoadministering to said mammal a formulation in an amount, at a frequency, and for a duration effective to prevent said non-invasive fungus-induced intestinal mucositis, said formulation comprising an antifungal agent.

40 ~~73.~~ A method for treating a mammal having a non-invasive fungus-induced intestinal mucositis, comprising the steps of:

a) identifying said mammal, and

b) mucoadministering to at least a portion of the digestive tract of said mammal a formulation in an amount, at a frequency, and for a duration effective to reduce or eliminate said non-invasive fungus-induced intestinal mucositis, said formulation comprising an antifungal agent, wherein said mucoadministration comprises orally applying said formulation to said digestive tract, and wherein said duration is greater than about 30 days.

41 ~~74.~~ A method for prophylactically treating a mammal at risk for developing non-invasive fungus-induced intestinal mucositis, comprising the steps of:

a) identifying said mammal, and

b) mucoadministering to at least a portion of the digestive tract of said mammal a formulation in an amount, at a frequency, and for a duration effective to prevent said non-invasive fungus-induced intestinal mucositis, said formulation comprising an antifungal agent.

42 75. An article of manufacture, comprising packaging material and a formulation contained within said packaging material, wherein said formulation comprises an antifungal agent and wherein said packaging material comprises a label or package insert indicating that said formulation can be mucoadministered to a mammal having non-invasive fungus-induced intestinal mucositis in an amount, at a frequency, and for a duration effective to reduce or eliminate said non-invasive fungus-induced intestinal mucositis.

43 76. An article of manufacture, comprising packaging material and a formulation contained within said packaging material, wherein said formulation comprises an antifungal agent and wherein said packaging material comprises a label or package insert indicating that said formulation can be mucoadministered to a mammal at risk for developing non-invasive fungus-induced intestinal mucositis in an amount, at a frequency, and for a duration effective to prevent said non-invasive fungus-induced intestinal mucositis.

B3 cont. 44 77. A method for treating a human having non-invasive fungus-induced intestinal mucositis, comprising mucoadministering to the digestive tract of said human a formulation in an amount, at a frequency, and for a duration effective to reduce or eliminate said non-invasive fungus-induced intestinal mucositis, said formulation comprising an antifungal agent, wherein said mucoadministration comprises orally applying said formulation to said digestive tract, and wherein said frequency is from about twice a day to about once a week.

45 78. The method of claim 44, wherein said human is immunocompetent.

46 79. The method of claim 44, wherein said non-invasive fungus-induced intestinal mucositis is characterized by polyp formation or polypoid change.

47 80. The method of claim 44, wherein said formulation is in the form of a capsule.

48 81. The method of claim 47, wherein said capsule is a regulated release capsule.

49 48
~~82.~~ The method of claim ~~81~~, wherein said regulated release capsule is a pH regulated release capsule.

50 48
~~83.~~ The method of claim ~~81~~, wherein said regulated release capsule is a time regulated release capsule.

51 44
~~84.~~ The method of claim ~~77~~, wherein said mucoadministration is a direct mucoadministration.

52 44
~~85.~~ The method of claim ~~77~~, wherein said antifungal agent comprises an azole.

53 44
~~86.~~ The method of claim ~~77~~, wherein said antifungal agent comprises an antifungal agent selected from the group consisting of ketoconazole, itraconazole, saperconazole, voriconazole, flucytosine, miconazole, fluconazole, griseofulvin, clotrimazole, econazole, terconazole, butoconazole, oxiconazole, sulconazole, ciclopirox olamine, haloprogin, tolnaftate, naftifine, terbinafine hydrochloride, morpholines, nystatin, natamycin, butenafine, undecylenic acid, Whitefield's ointment, propionic acid, and caprylic acid.

53 cont.

54 44
~~87.~~ The method of claim ~~77~~, wherein said antifungal agent comprises an antifungal agent selected from the group consisting of ketoconazole, itraconazole, saperconazole, and voriconazole.

55 44
~~88.~~ The method of claim ~~77~~, wherein said antifungal agent comprises amphotericin B.

56 44
~~89.~~ The method of claim ~~77~~, wherein said antifungal agent comprises itraconazole.

57 44
~~90.~~ The method of claim ~~77~~, wherein said formulation comprises about 0.01 ng to about 1000 mg of said antifungal agent.

58 91. The method of claim 44, wherein said formulation comprises a plurality of antifungal agents.

59 92. The method of claim 44, wherein said effective amount of said formulation comprises about 0.01 ng to about 1000 mg of said antifungal agent per kg of body weight of said human.

60 93. The method of claim 44, wherein said effective amount of said formulation comprises about 1 ng to about 500 mg of said antifungal agent per kg of body weight of said human.

61 94. The method of claim 44, wherein said effective amount of said formulation remains constant during said effective duration.

62 95. The method of claim 44, wherein said effective duration is greater than about 7 days.

63 96. The method of claim 44, wherein said effective duration is greater than about 14 days.

64 97. The method of claim 44, wherein said effective duration is greater than about 30 days.

65 98. The method of claim 44, wherein said effective duration is greater than about 60 days.

66 99. The method of claim 44, wherein said effective duration is greater than about 90 days.

67 100. The method of claim 44, wherein said formulation comprises a compound selected from the group consisting of pharmaceutically acceptable aqueous vehicles, pharmaceutically acceptable solid vehicles, mucolytic agents, antibacterial agents, anti-inflammatory agents, immunosuppressants, dilators, vaso-constrictors, steroids, and therapeutic compounds.

68 101. The method of claim 44, wherein said method comprises administering to said human a second formulation.

B3 cont

102. The method of claim 101, wherein said second formulation comprises a compound selected from the group consisting of antifungal agents, pharmaceutically acceptable aqueous vehicles, pharmaceutically acceptable solid vehicles, mucolytic agents, antibacterial agents, anti-inflammatory agents, immunosuppressants, dilators, vaso-constrictors, steroids, and therapeutic compounds.

103. The method of claim 77, said method comprising, after said mucoadministration, prophylactically mucoadministering to said human a prophylactic formulation in an amount, at a frequency, and for a duration effective to prevent said non-invasive fungus-induced intestinal mucositis, said prophylactic formulation comprising an antifungal agent.

104. The method of claim 103, wherein said prophylactic mucoadministration comprises direct mucoadministration.

REMARKS

Claims 1-20 of the above-identified application have been rejected. Applicant has cancelled claims 8, 14, and 15 without prejudice, and added claims 51-104 herein. Thus, claims 1-7, 9-13, 16-20, and 51-104 are pending. In addition, Applicant has amended claims 1 and 7 herein to more particularly point out and distinctly claim the subject matter Applicant regards as his invention. These amendments are supported throughout the specification as originally filed. For example, original claim 14 recites that the mucoadministration comprises orally applying the formulation to the digestive tract of the mammal, and original claim 37 recites that the duration is greater than about 30 days. Thus, these amendments do not add new matter. In light of these amendments and the remarks below, Applicant respectfully submits that the pending claims are in condition for allowance and free from the prior art including Sait *et al.*, *Digestive Diseases*, 15(11):993-1002 (1970).

Rejection under 35 U.S.C. §103(a)

The Examiner rejected claims 1-20 under 35 U.S.C. §103(a) as being unpatentable over Eisen (U.S. Patent No. 5,310,545) or Ramos *et al.* (*Nutr. Cancer*, 28(2):212-217 (1997)).

Specifically, the Examiner stated that Eisen teaches the use of a combination containing steroids and antifungal agents to treat inflammatory disorders such as mucositis, and that Ramos *et al.* teach on oral administration of short-chain fatty acids used to reduce intestinal mucositis.

Applicant respectfully disagrees. The present claims recite treating or preventing non-invasive fungus-induced intestinal mucositis. The Eisen reference discloses swishing mouthwash to treat inflammatory diseases of the mouth. At no point does the Eisen reference disclose the treatment of any intestinal condition, let alone a non-invasive fungus-induced intestinal mucositis condition. In addition, the Eisen reference fails to suggest any method that can be used to treat or prevent non-invasive fungus-induced intestinal mucositis. In fact, the Eisen reference uses the term "intestinal" only twice, and in both cases the term is used to indicate that a preferred mouthwash should contain an antifungal agent that is poorly absorbed by mucosa of the intestinal tract. See, column 4, lines 41-49 of the Eisen reference. In light of these deficiencies, Applicant respectfully submits that the Eisen reference does not render the presently claimed invention obvious.

The Ramos *et al.* reference also fails to suggest treating or preventing non-invasive fungus-induced intestinal mucositis as presently claimed. In fact, the Ramos *et al.* reference discloses administering a short-chain fatty acid solution to mice such that inflammation and necrosis caused by cytarbine administration is reduced. The present claims recite treating or preventing non-invasive fungus-induced intestinal mucositis, not inflammation caused by cytarbine administration. In addition, claim 1 recites using a duration that is greater than about 30 days to reduce or eliminate non-invasive fungus-induced intestinal mucositis. At no point does the Ramos *et al.* reference suggest using such a duration to reduce or eliminate non-invasive fungus-induced intestinal mucositis. Again, the Ramos *et al.* reference simply discloses administering a short-chain fatty acid solution to reduce inflammation caused by cytarbine administration. Thus, Applicant respectfully submits that the Ramos *et al.* reference does not render the presently claimed invention obvious.

In light of the above, Applicant respectfully requests the withdrawal of the rejections under 35 U.S.C. §103(a).

CONCLUSION

Applicant submits that claims 1-7, 9-13, 16-20, and 51-104 are in condition for allowance, which action is requested. Filed herewith is a check in payment of the excess claims fees required by the above amendments and Petition for Automatic Extension with the required fee. Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: September 11, 2000

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TRANSMITTAL LETTER

Correspondence relating to this application is enclosed.

1. Amendment response to the Office Action mailed April 11, 2000 (10 pages);
2. Information Disclosure Statement (2 pages);
3. PTO-1449 form (1 page);
4. Four references;
5. Petition for Two-Month Extension of Time (1 page);
6. Check for $1060.00 ($630.00 for claims, $234.00 for Information Disclosure Statement and $190.00 for Petition for extension);
7. Postcard.

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Signature

Jill Huso
Typed or Printed Name of Person Signing Certificate

Please apply any charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: September 11, 2000

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